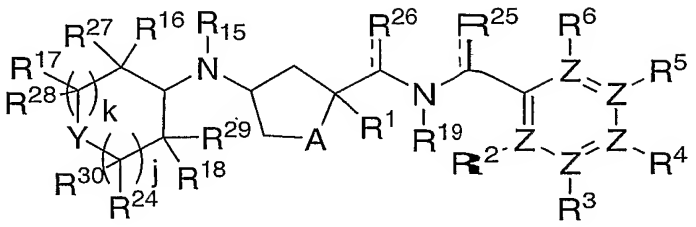
WHAT IS CLAIMED IS:

1. A compound of Formula I:



I

wherein:

A is selected from: -O-, -N(R^{20})-, -S-, -SO-, -SO_2-, -N(SO_2R^{14})-, and -N(COR^{13})-;

Y is selected from: -O-, -N(R^{20})-, -S-, -SO-, -SO_2-, -C(R^{21})(R^{22})—, -N(SO_2R^{14})-, -N(COR^{13})-, -C(R^{21})(COR^{11})-, -C(R^{21})($OCOR^{14}$)- and -CO-;

Z is C or N, where no more than three Z are N.

R^1 is selected from: hydrogen, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -S-C_{1-6}alkyl, -SO-C_{1-6}alkyl, -SO_2-C_{1-6}alkyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), -CN, -$NR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -O-CO-C_{1-6}alkyl, -O-CO_2-C_{1-6}alkyl, hydroxy, heterocycle and phenyl;

where said alkyl and cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -COR^{11}, -SO_2R^{14}, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -heterocycle, =O, -CN, phenyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO-C_{1-6}alkyl

unsubstituted or substituted with 1-6 fluoro, -SO_2-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro and -O-COR^{13},

where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR^{11}, C_{1-3}alkyl unsubstituted substituted with 1-6 fluoro, C_{1-3}alkoxy unsubstituted or substituted with 1-6 fluoro, NHCOH and NHCO(C_{1-3}alkyl);

R^2 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^2 is C, or R^2 is absent or is O when the Z bonded to R^2 is N;

R^3 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^3 is C, or R^3 is absent or is O when the Z bonded to R^3 is N;

R^4 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^4 is C, or R^4 is absent or is O when the Z bonded to R^4 is N;

R^5 is selected from: -heterocycle, -CN, -COR^{11}, C_{1-6}alkyl unsubstituted or substituted with one or more substituents selected from 1-6 fluoro and hydroxyl, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -CO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -pyridyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, fluoro, chloro, bromo, -C_{4-6}cycloalkyl, -O-C_{4-6}cycloalkyl, phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -O-phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro and -O-C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro, when the Z bonded to R^5 is C, or R^5 is absent or is O when the Z bonded to R^5 is N;

R^6 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^6 is C, or R^6 is absent or is O when the Z bonded to R^6 is N;

R^{11} is independently selected from: hydroxy, hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{12} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

or, separate R^{12} groups residing on the same or adjacent atoms together are C_{1-7}alkyl to form a ring, said C_{1-7}alkyl being unsubstituted or substituted with with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{13} is selected from: hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl and trifluoromethyl;

R^{14} is selected from: hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{15} is selected from: hydrogen and C_{1-6}alkyl, which is unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -CO_2H, -CO_2C_{1-6}alkyl, and-O-C_{1-3}alkyl;

R^{16} is selected from: hydrogen, C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: fluoro, C_{1-3}alkoxy, hydroxyl and $-COR^{11}$, fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, C_{3-6} cycloalkyl, -O-C_{3-6}cycloalkyl, hydroxy, $-COR^{11}$ and $-OCOR^{13}$;

or, R^{15} and R^{16} join to form a 5-7 membered ring where R^{15} and R^{16} together are C_{2-4}alkyl or C_{0-2}alkyl-O-C_{1-3}alkyl;

R^{17} is selected from: hydrogen, C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and $-COR^{11}$, COR^{11}, hydroxy, and -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxy, and $-COR^{11}$, or R^{17} is absent when R^{28} is O joined to a ring carbon via a double bond;

or, R^{16} and R^{17} join to form a 3-6 membered ring, where R^{16} and R^{17} together are C_{1-4}alkyl or C_{0-3}alkyl-O-C_{0-3}alkyl;

or, R^{24} and R^{17} join to form a 3-6 membered ring, where R^{24} and R^{17} together are C_{1-4}alkyl or C_{0-3}alkyl-O-C_{0-3}alkyl;

R^{18} is selected from: hydrogen, C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, fluoro, -O-C_{3-6}cycloalkyl and -O-C_{1-3}alkyl unsubstituted or substituted with 1-6 fluoro;

or, R^{16} and R^{18} join to form a 5-6 membered ring where R^{16} and R^{18} together are C_{2-3}alkyl, where said alkyl is unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxy, $-COR^{11}$, C_{1-3}alkyl, and C_{1-3}alkoxy;

or, R^{16} and R^{18} join to form a 6-8 membered ring, where R^{16} and R^{18} together are C_{1-2}alkyl-O-C_{1-2}alkyl, where said alkyl is unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxy, $-COR^{11}$, C_{1-3}alkyl and C_{1-3}alkoxy;

or, R^{16} and R^{18} join to form a 6-7 membered ring, where R^{16} and R^{18} together are-O-C_{1-2}alkyl-O-, where said alkyl is unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxy, -COR^{11}, C_{1-3}alkyl and C_{1-3}alkoxy;

R^{19} is selected from: hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;
or, R^2 and R^{19} join to form a heterocycle ring, where R^2 and R^{19} are selected from -$CH_2(CR^{31}R^{31})_{1-3}$-, -$CH_2$-$NR^{32}$-, -$NR^{20}$-$CR^{31}R^{31}$-, -$CH_2O$-, -$CH_2SO_2$-, -$CH_2SO$-, -$CH_2S$- and -$CR^{31}R^{31}$-;

R^{20} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, C_{3-6} cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{21} and R^{22} are independently selected from: hydrogen, hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;
R^{24} is selected from: hydrogen, COR^{11}, hydroxyl, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxy, and -COR^{11}, and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and -COR^{11};

R^{25} and R^{26} are independently selected from: =O, hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;

R^{27}, R^{28}, R^{29}, and R^{30} are independently selected from: hydrogen, COR^{11}, hydroxy, C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and -COR^{11}, and -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and -COR^{11};

R^{31} is independently selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxy, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$, hydroxy, halo, $-NR^{12}R^{12}$, $-COR^{11}$, $-CONR^{12}R^{12}$, $-NR^{12}COR^{13}$, $-OCONR^{12}R^{12}$, $-NR^{12}CONR^{12}R^{12}$, -heterocycle, -CN, $-NR^{12}-SO_2-NR^{12}R^{12}$, $-NR^{12}-SO_2-R^{14}$, and $-SO_2-NR^{12}R^{12}$, or one R^{31} is =O when the other R^{31} is absent;

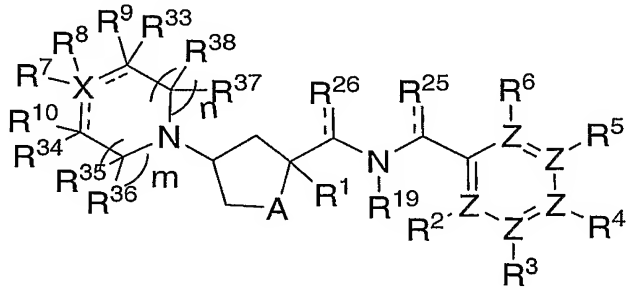
R^{32} is selected from: hydrogen, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$ and C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxyl;

j and k are independently 0, 1 or 2;

a dashed line represents an optional single bond, whereby a dashed line used in conjunction with a solid line represents either a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. A compound of Formula II:



II

wherein:

A is selected from: -O-, $-N(R^{20})-$, -S-, -SO-, $-SO_2-$, $-N(SO_2R^{14})-$, and $-N(COR^{13})-$;

X is selected from O, N, S, SO_2 and C;

Z is C or N, where no more than three Z are N.

R^1 is selected from: hydrogen, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -S-C_{1-6}alkyl, -SO-C_{1-6}alkyl, -SO_2-C_{1-6}alkyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), -CN, -$NR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -O-CO-C_{1-6}alkyl, -O-CO_2-C_{1-6}alkyl, hydroxy, heterocycle and phenyl;

where said alkyl and cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -COR^{11}, -SO_2R^{14}, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -heterocycle, =O, -CN, phenyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO_2-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro and -O-COR^{13},

where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR^{11}, C_{1-3}alkyl unsubstituted substituted with 1-6 fluoro, C_{1-3}alkoxy unsubstituted or substituted with 1-6 fluoro, NHCOH and NHCO(C_{1-3}alkyl);

R^2 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^2 is C, or R^2 is absent or is O when the Z bonded to R^2 is N;

R^3 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^3 is C, or R^3 is absent or is O when the Z bonded to R^3 is N;

R^4 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^4 is C, or R^4 is absent or is O when the Z bonded to R^4 is N;

R^5 is selected from: C_{1-6}alkyl unsubstituted or substituted with one or more substituents selected from 1-6 fluoro and hydroxyl, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -CO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -pyridyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, fluoro, chloro, bromo, -C_{4-6}cycloalkyl, -O-C_{4-6}cycloalkyl, phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -O-phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro, -O-C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro, -heterocycle, -CN and -COR^{11}, when the Z bonded to R^5 is C, or R^5 is absent or is O when the Z bonded to R^5 is N;

R^6 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^6 is C, or R^6 is absent or is O when the Z bonded to R^6 is N;

R^7 is selected from: hydrogen, (C_{0-6}alkyl)-phenyl, (C_{0-6}alkyl)-heterocycle, (C_{0-6}alkyl)-C_{3-7}cycloalkyl , (C_{0-6}alkyl)-COR^{11}, (C_{0-6}alkyl)-(alkene)-COR^{11}, (C_{0-6}alkyl)-SO_3H, (C_{0-6}alkyl)-W-C_{0-4}alkyl, (C_{0-6}alkyl)-$CONR^{12}$-phenyl and (C_{0-6}alkyl)-$CONR^{23}$-V-COR^{11}, when X is C or N, or R^7 is absent when X is O, S, or SO_2,

where W is selected from: a single bond, -O-, -S-, -SO-, -SO_2-, -CO-, -CO_2-, -$CONR^{12}$- and-NR^{12}-,

where V is selected from C_{1-6}alkyl and phenyl,

where said C_{0-6}alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, hydroxy, -C_{0-6}alkyl, -O-C_{1-3}alkyl, trifluoromethyl and -C_{0-2}alkyl-phenyl,

where said phenyl, heterocycle, cycloalkyl or C_{0-4}alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-COR^{11}, -CN, -$NR^{12}R^{12}$, -$CONR^{12}R^{12}$ and -C_{0-3}-heterocycle, or said phenyl or said heterocycle is fused to a second heterocycle, said second heterocycle being unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, -COR^{11}, and–C_{1-3}alkyl,

where said alkene is unsubstituted or substituted with 1-3 substituents independently selected from halo, trifluoromethyl, C_{1-3}alkyl, phenyl and heterocycle;

R^8 is selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, -COR^{11}, -$CONR^{12}R^{12}$ and–CN, when X is C, or R^8 is absent when X is O, S, SO_2 or N or when a double bond joins the carbons to which R^7 and R^{10} are attached;

or, R^7 and R^8 join to form a ring selected from: 1H-indene, 2,3-dihydro-1H-indene, 2,3-dihydro-benzofuran, 1,3-dihydro-isobenzofuran, 2,3-dihydro-benzothiofuran, 1,3-dihydro-isobenzothiofuran, 6*H*-cyclopenta[*d*]isoxazol-3-ol, cyclopentane and cyclohexane, where said ring is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl,-C_{0-3}-COR^{11}, -CN, -$NR^{12}R^{12}$, -$CONR^{12}R^{12}$ and -C_{0-3}-heterocycle;

R^9 and R^{10} are independently selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, =O, and halo;

or, R^7 and R^9, or R^8 and R^{10}, join to form a ring which is phenyl or heterocycle,
wherein said ring is unsubstituted or substituted with 1-7 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -COR^{11}, -CN, -$NR^{12}R^{12}$ and -$CONR^{12}R^{12}$;

R^{11} is independently selected from: hydroxy, hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{12} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

or, separate R^{12} groups residing on the same or adjacent atoms together are C_{1-7}alkyl to form a ring, said C_{1-7}alkyl being unsubstituted or substituted with with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{13} is selected from: hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl and trifluoromethyl;

R^{14} is selected from: hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{19} is selected from: hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;

or, R^2 and R^{19} join to form a heterocycle ring, where R^2 and R^{19} are selected from -$CH_2(CR^{31}R^{31})_{1-3}$-, -$CH_2$-$NR^{32}$-, -$NR^{20}$-$CR^{31}R^{31}$-, -$CH_2O$-, -$CH_2SO_2$-, -$CH_2SO$-, -$CH_2S$- and -$CR^{31}R^{31}$-;

R^{20} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, C_{3-6} cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-6 substituents where the

substituents are independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{23} is hydrogen or C_{1-4}alkyl, or where R^{23} is joined via C_{1-5}alkyl to one of the carbons of V to form a ring;

R^{25} and R^{26} are independently selected from: =O, hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;

R^{31} is independently selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxy, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$, hydroxy, halo, -$NR^{12}R^{12}$, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$OCONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -heterocycle, -CN, -NR^{12}-SO_2-$NR^{12}R^{12}$, -NR^{12}-SO_2-R^{14}, -SO_2-$NR^{12}R^{12}$, and =O ;

R^{32} is selected from: hydrogen, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$ and C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxyl;

R^{33} and R^{34} are independently selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, trifluoromethyl and halo, or R^{33} and R^{34} are absent when the carbon to which they are bound unsaturated;

R^{35} and R^{38} are independently selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, trifluoromethyl and halo;

R^{36} and R^{37} are independently selected from: hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, halo and hydrogen, where said alkyl is unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxyl;

or, R^{36} and R^{37} join to form a ring, where R^{36} and R^{37} together are selected from -C_{1-4}alkyl-, -C_{0-2}alkyl-O-C_{1-3}alkyl- and–C_{1-3}alkyl-O-C_{0-2}alkyl-; where said alkyls are unsubstituted or substituted with 1-2 substituents selected from of oxy, fluoro, hydroxy, methoxy, methyl or trifluoromethyl;

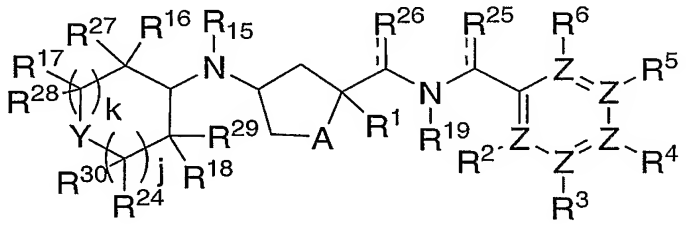
m is 0, 1 or 2;

n is 1 or 2;

a dashed line represents an optional single bond, whereby a dashed line used in conjunction with a solid line represents either a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

3. A compound of Formula I:



I

wherein:

A is selected from: -O-, -N(R^{20})-, -S-, -SO-, -SO_2-, -N(SO_2R^{14})-, and -N(COR^{13})-;

Y is selected from: -O-, -N(R^{20})-, -S-, -SO-, -SO_2-, -C(R^{21})(R^{22})-, -N(SO_2R^{14})-, -N(COR^{13})-, -C(R^{21})(COR^{11})-, -C(R^{21})($OCOR^{14}$)- and -CO-;

Z is C or N, where no more than three Z are N.

R^1 is selected from: hydrogen, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -S-C_{1-6}alkyl, -SO-C_{1-6}alkyl, -SO_2-C_{1-6}alkyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), -CN, -$NR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -O-CO-C_{1-6}alkyl, -O-CO_2-C_{1-6}alkyl, hydroxy, heterocycle and phenyl;

where said alkyl and cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -COR^{11}, -SO_2R^{14}, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -heterocycle, =O, -CN, phenyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO_2-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro and -O-COR^{13},

where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR^{11}, C_{1-3}alkyl unsubstituted or substituted with 1-6 fluoro, and C_{1-3}alkoxy unsubstituted or substituted with 1-6 fluoro;

R^2 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^2 is C, or R^2 is absent or is O when the Z bonded to R^2 is N;

R^3 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^3 is C, or R^3 is absent or is O when the Z bonded to R^3 is N;

R^4 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^4 is C, or R^4 is absent or is O when the Z bonded to R^4 is N;

R^5 is selected from: -heterocycle, -CN, -COR^{11}, C_{1-6}alkyl unsubstituted or substituted with one or more substituents selected from 1-6 fluoro and hydroxyl, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -CO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -pyridyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, fluoro, chloro, bromo, -C_{4-6}cycloalkyl, -O-C_{4-6}cycloalkyl, phenyl unsubstituted or substituted with one or more substituents selected from halo,

trifluoromethyl, C_{1-4}alkyl and COR^{11}, -O-phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro and -O-C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro, when the Z bonded to R^5 is C, or R^5 is absent or is O when the Z bonded to R^5 is N;

R^6 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^6 is C, or R^6 is absent or is O when the Z bonded to R^6 is N;

R^{11} is independently selected from: hydroxy, hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{12} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

or, separate R^{12} groups residing on the same or adjacent atoms together are C_{1-7}alkyl to form a ring, said C_{1-7}alkyl being unsubstituted or substituted with with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{13} is selected from: hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl and trifluoromethyl;

R^{14} is selected from: hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{15} is selected from: hydrogen and C_{1-6}alkyl, which is unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, $-CO_2H$, $-CO_2C_{1-6}$alkyl, and–O-C_{1-3}alkyl;

R^{16} is selected from: hydrogen, C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: fluoro, C_{1-3}alkoxy, hydroxyl and $-COR^{11}$, fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, C_{3-6} cycloalkyl, -O-C_{3-6}cycloalkyl, hydroxy, $-COR^{11}$ and $-OCOR^{13}$;

or, R^{15} and R^{16} join to form a 5-7 membered ring where R^{15} and R^{16} together are C_{2-4}alkyl or C_{0-2}alkyl-O-C_{1-3}alkyl;

R^{17} is selected from: hydrogen, C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and $-COR^{11}$, COR^{11}, hydroxy, and -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxy, and $-COR^{11}$, or R^{17} is absent when R^{28} is O joined to a ring carbon via a double bond;

or, R^{16} and R^{17} join to form a 3-6 membered ring, where R^{16} and R^{17} together are C_{1-4}alkyl or C_{0-3}alkyl-O-C_{0-3}alkyl;

or, R^{24} and R^{17} join to form a 3-6 membered ring, where R^{24} and R^{17} together are C_{1-4}alkyl or C_{0-3}alkyl-O-C_{0-3}alkyl;

R^{18} is selected from: hydrogen, C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, fluoro, -O-C_{3-6}cycloalkyl and -O-C_{1-3}alkyl unsubstituted or substituted with 1-6 fluoro;

or, R^{16} and R^{18} join to form a 5-6 membered ring where R^{16} and R^{18} together are C_{2-3}alkyl, where said alkyl is unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxy, $-COR^{11}$, C_{1-3}alkyl, and C_{1-3}alkoxy;

or, R^{16} and R^{18} join to form a 6-8 membered ring, where R^{16} and R^{18} together are C_{1-2}alkyl-O-C_{1-2}alkyl, where said alkyl is unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxy, -COR^{11}, C_{1-3}alkyl and C_{1-3}alkoxy;

or, R^{16} and R^{18} join to form a 6-7 membered ring, where R^{16} and R^{18} together are-O-C_{1-2}alkyl-O-, where said alkyl is unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxy, -COR^{11}, C_{1-3}alkyl and C_{1-3}alkoxy;

R^{19} is selected from: hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;

or, R^2 and R^{19} join to form a heterocycle ring, where R^2 and R^{19} are selected from -$CH_2(CR^{31}R^{31})_{1-3}$-, -$CH_2$-$NR^{32}$-, -$NR^{20}$-$CR^{31}R^{31}$-, -$CH_2O$-, -$CH_2SO_2$-, -$CH_2SO$-, -$CH_2S$- and -$CR^{31}R^{31}$-;

R^{20} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, C_{3-6} cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{21} and R^{22} are independently selected from: hydrogen, hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{24} is selected from: hydrogen, COR^{11}, hydroxyl, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxy, and -COR^{11}, and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and -COR^{11};

R^{25} and R^{26} are independently selected from: =O, hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;

R^{27}, R^{28}, R^{29}, and R^{30} are independently selected from: hydrogen, COR^{11}, hydroxy, C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and $-COR^{11}$, and $-O-C_{1-6}$alkyl unsubstituted or substituted with 1-6 substituents selected from fluoro, C_{1-3}alkoxy, hydroxyl and $-COR^{11}$;

R^{31} is independently selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxy, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$, hydroxy, halo, $-NR^{12}R^{12}$, $-COR^{11}$, $-CONR^{12}R^{12}$, $-NR^{12}COR^{13}$, $-OCONR^{12}R^{12}$, $-NR^{12}CONR^{12}R^{12}$, -heterocycle, -CN, $-NR^{12}-SO_2-NR^{12}R^{12}$, $-NR^{12}-SO_2-R^{14}$, and $-SO_2-NR^{12}R^{12}$, or one R^{31} is =O when the other R^{31} is absent;

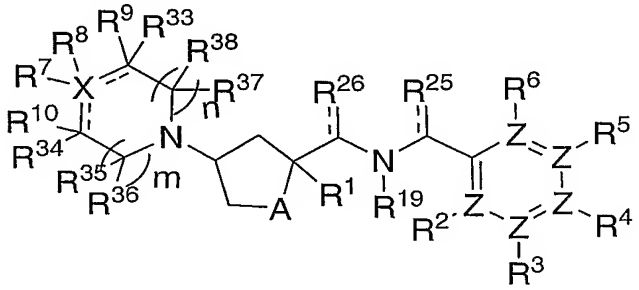
R^{32} is selected from: hydrogen, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$ and C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxyl;

j and k are independently 0, 1 or 2;

a dashed line represents an optional single bond, whereby a dashed line used in conjunction with a solid line represents either a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

4. A compound of Formula II:



II

wherein:

A is selected from: -O-, -N(R^{20})-, -S-, -SO-, -SO_2-, -N(SO_2R^{14})-, and -N(COR^{13})-;

X is selected from O, N, S, SO_2 and C;

Z is C or N, where no more than three Z are N;

R^1 is selected from: hydrogen, -C_{1-6}alkyl, -O-C_{1-6}alkyl, -S-C_{1-6}alkyl, -SO-C_{1-6}alkyl, -SO_2-C_{1-6}alkyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), -CN, -$NR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -O-CO-C_{1-6}alkyl, -O-CO_2-C_{1-6}alkyl, hydroxy, heterocycle and phenyl;

where said alkyl and cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -$CONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -COR^{11}, -SO_2R^{14}, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -heterocycle, =O, -CN, phenyl, -$SO_2NR^{12}R^{12}$, -NR^{12}-SO_2-$NR^{12}R^{12}$, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -SO_2-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro and -O-COR^{13},

where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR^{11}, C_{1-3}alkyl unsubstituted substituted with 1-6 fluoro, and C_{1-3}alkoxy unsubstituted or substituted with 1-6 fluoro;

R^2 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^2 is C, or R^2 is absent or is O when the Z bonded to R^2 is N;

R^3 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^3 is C, or R^3 is absent or is O when the Z bonded to R^3 is N;

R^4 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^4 is C, or R^4 is absent or is O when the Z bonded to R^4 is N;

R^5 is selected from: C_{1-6}alkyl unsubstituted or substituted with one or more substituents selected from 1-6 fluoro and hydroxyl, -O-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -CO-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -S-C_{1-6}alkyl unsubstituted or substituted with 1-6 fluoro, -pyridyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, fluoro, chloro, bromo, -C_{4-6}cycloalkyl, -O-C_{4-6}cycloalkyl, phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -O-phenyl unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl and COR^{11}, -C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro, -O-C_{3-6}cycloalkyl unsubstituted or substituted with 1-6 fluoro, -heterocycle, -CN and -COR^{11}, when the Z bonded to R^5 is C, or R^5 is absent or is O when the Z bonded to R^5 is N;

R^6 is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, -O-C_{1-3}alkyl unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl and heterocycle, when the Z bonded to R^6 is C, or R^6 is absent or is O when the Z bonded to R^6 is N;

R^7 is selected from: hydrogen, (C_{0-6}alkyl)-phenyl, (C_{0-6}alkyl)-heterocycle, (C_{0-6}alkyl)-C_{3-7}cycloalkyl, (C_{0-6}alkyl)-COR^{11}, (C_{0-6}alkyl)-(alkene)-COR^{11}, (C_{0-6}alkyl)-SO_3H, (C_{0-6}alkyl)-W-C_{0-4}alkyl, (C_{0-6}alkyl)-$CONR^{12}$-phenyl and (C_{0-6}alkyl)-$CONR^{23}$-V-COR^{11}, when X is C or N, or R^7 is absent when X is O, S, or SO_2,

where W is selected from: a single bond, -O-, -S-, -SO-, -SO_2-, -CO-, -CO_2-, -$CONR^{12}$- and -NR^{12}-,

where V is selected from C_{1-6}alkyl and phenyl,

where said C_{0-6}alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, hydroxy, -C_{0-6}alkyl, -O-C_{1-3}alkyl, trifluoromethyl and -C_{0-2}alkyl-phenyl,

where said phenyl, heterocycle, cycloalkyl or C_{0-4}alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -C_{0-3}-COR^{11}, -CN, -$NR^{12}R^{12}$, -$CONR^{12}R^{12}$ and -C_{0-3}-heterocycle, or said phenyl or said heterocycle is fused to a second heterocycle, said second heterocycle being unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, -COR^{11}, and–C_{1-3}alkyl,

where said alkene is unsubstituted or substituted with 1-3 substituents independently selected from halo, trifluoromethyl, C_{1-3}alkyl, phenyl and heterocycle;

R^8 is selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, -COR^{11}, -$CONR^{12}R^{12}$ and–CN, when X is C, or R^8 is absent when X is O, S, SO_2 or N or when a double bond joins the carbons to which R^7 and R^{10} are attached;

or, R^7 and R^8 join to form a ring selected from: 1H-indene, 2,3-dihydro-1H-indene, 2,3-dihydro-benzofuran, 1,3-dihydro-isobenzofuran, 2,3-dihydro-benzothiofuran, 1,3-dihydro-isobenzothiofuran, 6*H*-cyclopenta[*d*]isoxazol-3-ol, cyclopentane and cyclohexane, where said ring is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl,-C_{0-3}-COR^{11}, -CN, -$NR^{12}R^{12}$, -$CONR^{12}R^{12}$ and -C_{0-3}-heterocycle;

R^9 and R^{10} are independently selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, -O-C_{1-3}alkyl, =O, and halo;

or, R^7 and R^9, or R^8 and R^{10}, join to form a ring which is phenyl or heterocycle,

wherein said ring is unsubstituted or substituted with 1-7 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -COR^{11}, -CN, -$NR^{12}R^{12}$ and -$CONR^{12}R^{12}$;

R^{11} is independently selected from: hydroxy, hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{12} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

or, separate R^{12} groups residing on the same or adjacent atoms together are C_{1-7}alkyl to form a ring, said C_{1-7}alkyl being unsubstituted or substituted with with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{13} is selected from: hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl and trifluoromethyl;

R^{14} is selected from: hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6} alkyl, and trifluoromethyl;

R^{19} is selected from: hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: -COR^{11}, hydroxy, fluoro, chloro and -O-C_{1-3}alkyl;

or, R^2 and R^{19} join to form a heterocycle ring, where R^2 and R^{19} are selected from -$CH_2(CR^{31}R^{31})_{1-3}$-, -$CH_2$-$NR^{32}$-, -$NR^{20}$-$CR^{31}R^{31}$-, -$CH_2O$-, -$CH_2SO_2$-, -$CH_2SO$-, -$CH_2S$- and -$CR^{31}R^{31}$-;

R^{20} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, C_{3-6} cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$ alkyl, and trifluoromethyl;

R^{23} is hydrogen or C_{1-4}alkyl, or where R^{23} is joined via C_{1-5}alkyl to one of the carbons of V to form a ring;

R^{25} and R^{26} are independently selected from: =O, hydrogen, phenyl and C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from: $-COR^{11}$, hydroxy, fluoro, chloro and $-O-C_{1-3}$alkyl;

R^{31} is independently selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxy, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$, hydroxy, halo, $-NR^{12}R^{12}$, $-COR^{11}$, $-CONR^{12}R^{12}$, $-NR^{12}COR^{13}$, $-OCONR^{12}R^{12}$, $-NR^{12}CONR^{12}R^{12}$, -heterocycle, -CN, $-NR^{12}-SO_2-NR^{12}R^{12}$, $-NR^{12}-SO_2-R^{14}$, $-SO_2-NR^{12}R^{12}$, and =O ;

R^{32} is selected from: hydrogen, COR^{13}, SO_2R^{14}, $SO_2NR^{12}R^{12}$ and C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxyl;

R^{33} and R^{34} are independently selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, $-O-C_{1-3}$alkyl, trifluoromethyl and halo, or R^{33} and R^{34} are absent when the carbon to which they are bound unsaturated;

R^{35} and R^{38} are independently selected from: hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, $-O-C_{1-3}$alkyl, trifluoromethyl and halo;

R^{36} and R^{37} are independently selected from: hydroxy, C_{1-6}alkyl, C_{1-6}alkyl-COR^{11}, C_{1-6}alkyl-hydroxy, $-O-C_{1-3}$alkyl, halo and hydrogen, where said alkyl is unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxyl;

or, R^{36} and R^{37} join to form a ring, where R^{36} and R^{37} together are selected from -C_{1-4}alkyl-, -C_{0-2}alkyl-O-C_{1-3}alkyl- and–C_{1-3}alkyl-O-C_{0-2}alkyl-; where said alkyls are unsubstituted or substituted with 1-2 substituents selected from of oxy, fluoro, hydroxy, methoxy, methyl or trifluoromethyl;

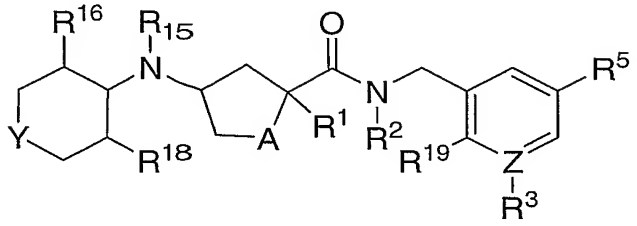
m is 0, 1 or 2;

n is 1 or 2;

a dashed line represents an optional single bond, whereby a dashed line used in conjunction with a solid line represents either a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

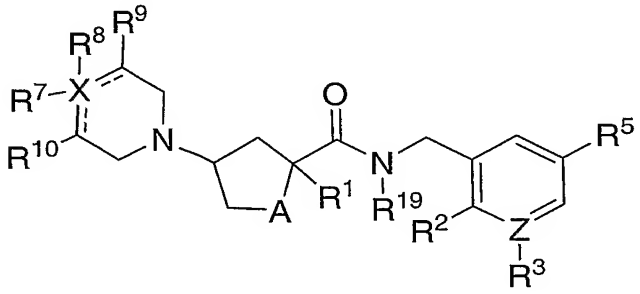
5. The compound of claim 1 having the Formula Ia:



Ia

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

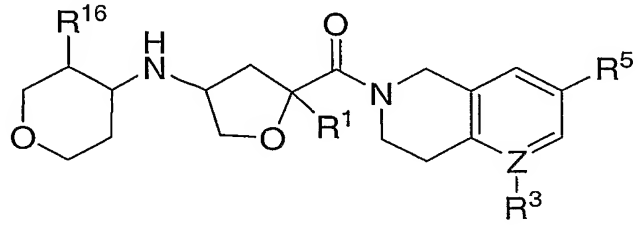
6. The compound of claim 2 having the Formula IIa:



IIa

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

7. The compound of claim 1 having the Formula Ib:



Ib

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

8. The compound of claim 1, wherein A is N or O.

9. The compound of claim 2, wherein A is N or O.

10. The compound of claim 2, wherein X is N, O or C.

11. The compound of claim 1, wherein Y is O or C.

12. The compound of claim 1, wherein Z is N or C.

13. The compound of claim 2, wherein Z is N or C.

14. The compound of claim 1, wherein R^1 is selected from: -C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents independently selected from halo, hydroxy, -O-C_{1-3}alkyl and trifluoromethyl, -C_{0-6}alkyl-O-C_{1-6}alkyl- unsubstituted or substituted with 1-6 substituents independently selected from halo and trifluoromethyl, -C_{0-6}alkyl-S-C_{1-6}alkyl- unsubstituted or substituted with 1-6 substituents independently selected from halo and trifluoromethyl, -(C_{3-5}cycloalkyl)-(C_{0-6}alkyl) unsubstituted or substituted with 1-7 substituents independently selected from halo, hydroxy, -O-C_{1-3}alkyl and trifluoromethyl, phenyl unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxyl, C_{1-3}alkyl, C_{1-3}alkoxy and trifluoromethyl, and heterocycle unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxyl, C_{1-3}alkyl, C_{1-3}alkoxy and trifluoromethyl.

15. The compound of claim 2, wherein R^1 is selected from: -C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents independently selected from halo, hydroxy, -O-C_{1-3}alkyl and trifluoromethyl, -C_{0-6}alkyl-O-C_{1-6}alkyl- unsubstituted or substituted with 1-6 substituents independently selected from halo and trifluoromethyl, -C_{0-6}alkyl-S-C_{1-6}alkyl- unsubstituted or substituted with 1-6 substituents independently selected from halo and trifluoromethyl, -(C_{3-5}cycloalkyl)-(C_{0-6}alkyl) unsubstituted or substituted with 1-7 substituents independently selected from halo, hydroxy, -O-C_{1-3}alkyl and trifluoromethyl, phenyl unsubstituted or substituted with 1-3 substituents independently

selected from halo, hydroxyl, C_{1-3}alkyl, C_{1-3}alkoxy and trifluoromethyl, and heterocycle unsubstituted or substituted with 1-3 substituents independently selected from halo, hydroxyl, C_{1-3}alkyl, C_{1-3}alkoxy and trifluoromethyl.

16. The compound of claim 1, wherein R^2 is H, or wherein R^2 and R^{19} together are C_2-alkyl.

17. The compound of claim 2, wherein R^2 is H, or wherein R^2 and R^{19} together are C_2-alkyl.

18. The compound of claim 1, wherein when Z is C, R^3 is selected from: hydrogen, trifluoromethyl, trifluoromethoxy, hydroxy, chloro, fluoro, bromo and phenyl.

19. The compound of claim 2, wherein when Z is C, R^3 is selected from: hydrogen, trifluoromethyl, trifluoromethoxy, hydroxy, chloro, fluoro, bromo and phenyl.

20. The compound of claim 1, wherein when when Z is N, R^3 is O or is absent.

21. The compound of claim 2, wherein when when Z is N, R^3 is O or is absent.

22. The compound of claim 1, wherein when R^5 is selected from: hydrogen, trifluoromethyl, trifluoromethoxy, hydroxy, chloro, fluoro, bromo and phenyl.

23. The compound of claim 2, wherein when R^5 is selected from: hydrogen, trifluoromethyl, trifluoromethoxy, hydroxy, chloro, fluoro, bromo and phenyl.

24. The compound of claim 2, wherein R^7 is selected from phenyl, heterocycle, C_{3-7}cycloalkyl, C_{1-6}alkyl,–COR^{11} and -CONH-V-COR^{11}, where V is C_{1-6}alkyl or phenyl, and where said phenyl, heterocycle, C_{3-7}cycloalkyl and C_{1-6}alkyl are unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -COR^{11}, -CN, -heterocycle and -$CONR^{12}R^{12}$.

25. The compound of claim 2, wherein R^7 is selected from phenyl, heterocycle, C_{1-4}alkyl,–COR^{11} and -CONH-V-COR^{11}, where V is C_{1-6}alkyl or phenyl, and where siad phenyl, heterocycle, and C_{1-4}alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -COR^{11} and –heterocycle.

26. The compound of claim 2, wherein R^7 is selected from: hydrogen, -COR^{11}, -$CONHCH_3$, phenyl and heterocycle.

27. The compound of claim 2, wherein when X is C, R^8 is selected from: hydrogen, hydroxy, -CN, and fluoro.

28. The compound of claim 2, wherein R^7 and R^8 join to form a ring selected from 1H-indene and 2,3-dihydro-1H-indene, where said ring is unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, -O-C_{1-3}alkyl, -COR^{11} and -heterocycle.

29. The compound of claim 2, wherein R^9 and R^{10} are independently selected from: hydrogen, hydroxy, -CH_3, -O-CH_3 and =O.

In certain embodiments of the present invention R^{16} is selected from: hydrogen, -O-C_{1-3}alkyl, fluoro, hydroxyl, and C_{1-3}alkyl unsubstituted or substituted with 1-6 fluoro.

30. The compound of claim 1, wherein R^{16} is selected from: hydrogen, trifluoromethyl, methyl, methoxy, ethoxy, ethyl, fluoro and hydroxy.

31. The compound of claim 1, wherein R^{18} is selected from: hydrogen, methyl and methoxy.

32. The compound of claim 1, wherein R^{16} and R^{18} together are -CH_2CH_2- or -$CH_2CH_2CH_2$-.

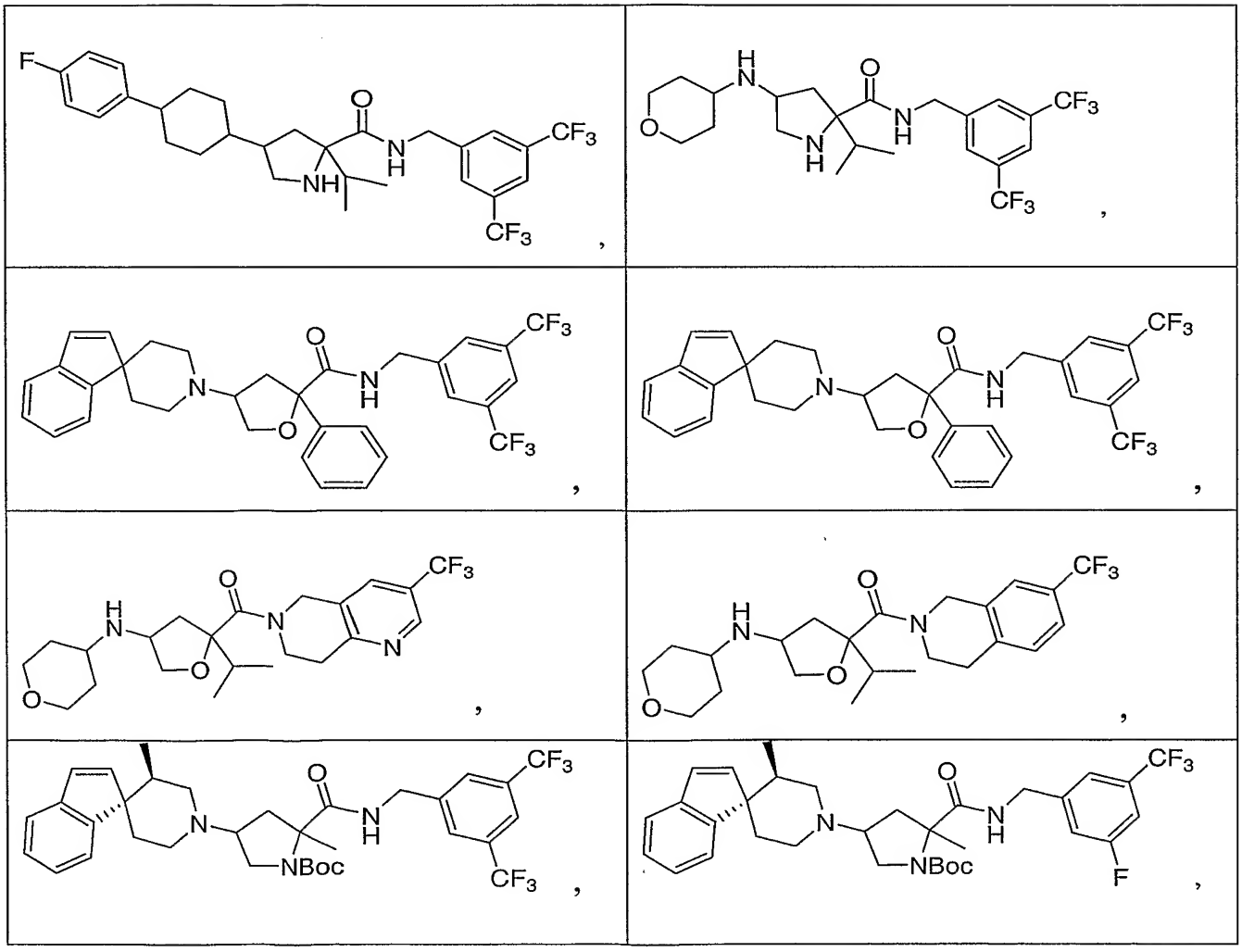
33. The compound of claim 1, wherein R^{26} is =O.

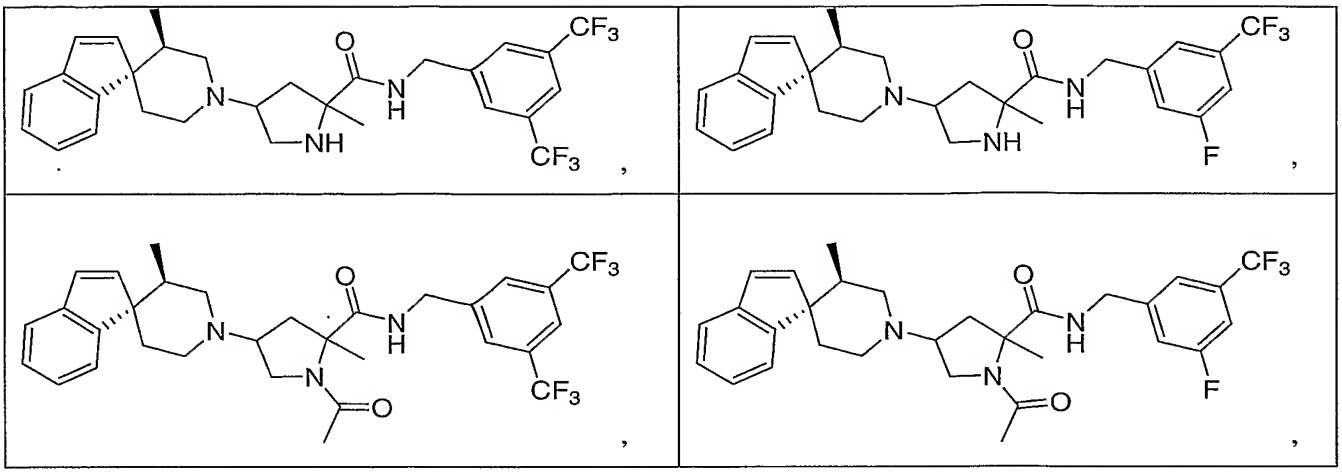
34. The compound of claim 1, wherein R^{26} is =O.

35. The compound of claim 2, wherein m is 0 or 1.

36. The compound of claim 2, wherein n is 1 or 2.

37. A compound selected from:





and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

38. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

39. A method for modulations of chemokine receptor activity in a mammal which comprises the administration of an effective amount of a compound of Claim 1.

40. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the administration to a patient of an effective amount of a compound of Claim 1.

41. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of a compound of Claim 1.

42. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 2.

43. A method for modulations of chemokine receptor activity in a mammal which comprises the administration of an effective amount of a compound of Claim 2.

44. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the administration to a patient of an effective amount of a compound of Claim 2.

45. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of a compound of Claim 2.